Management of Clinically Localized Prostate Cancer

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Critics of screening have stated that early detection of prostate cancer does not necessarily reflect a diminishing death rate from the disease. However, several recent reports have demonstrated that the death rate from prostate cancer is decreasing, representing the most compelling validation for aggressive screening. Prostate cancer can be halted only if there is no evidence of systemic or regional metastases and the disease is confined to the surgical field or the radiation template. Surgeons and radiation oncologists must make a concerted effort to exclude men with regional and systemic metastases who are unlikely to benefit from treatment. With the widespread acceptance of prostate-specific antigen screening, a greater proportion of men are being diagnosed with clinically localized prostate cancer. Both radical prostatectomy and radiation therapy are able to halt disease spread in this significant subset of men, but survival outcomes indicate that radical prostatectomy is a more reliable treatment than radiation therapy for clinically localized prostate cancer. Overall, the immediate treatment-related morbidity of radical prostatectomy and radiation therapy in the modern era is quite low. Radical prostatectomy and radiation therapy appear to have a similar impact on continence and erectile function. There is a need for neoadjuvant and adjuvant therapies that can be utilized in those cases where radical prostatectomy and radiation are less likely to completely eradicate or destroy the cancer.

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Key words: Prostate cancer • Prostate-specific antigen • Gleason score • Radical prostatectomy

Prostate cancer represents the second most common cause of cancer-related death in American males.[1] At the present time, there are no hormonal, immunological, or chemotherapeutic regimens that reliably treat advanced prostate cancers. Therefore the death rate from prostate cancer can be reduced by diagnosing a greater proportion of early prostate cancers at a stage when they

are amenable to localized therapies or by developing effective therapies for recurrent and advanced disease. It is intuitive that increasing the detection rate of clinically localized prostate cancers should result in decreasing the rate of cancer deaths secondary to prostate cancer. Over the last decade, screening for prostate cancer utilizing both serum prostate-specific antigen (PSA) and digital rectal examination has become widely accepted. As a result of screening, there has been a dramatic stage migration favoring the detection of clinically localized disease.[2,3]

Table 1
Prostate Cancer Survival Statistics for American Males

	Probability of Survival (%)			
Baseline Age	5 Years	10 Years	15 Years	20 Years
50	96	90	82	71
55	94	85	74	60
60	91	79	64	46
65	87	70	50	29
70	81	58	34	15
75	72	42	18	5

Source: U.S. Department of Health and Human Services. *Vital Statistics of the United States.* Hyattsville, Md: U.S. National Center for Health Statistics; 1989.

Critics of screening have stated that early detection does not necessarily reflect a diminishing death rate from the disease. However, several recent reports have demonstrated that the death rate from prostate cancer is decreasing.[4,5] The decreasing death rate from prostate cancer represents the most compelling validation for aggressive screening. The development of effective treatment for recurrent or advanced disease remains a significant challenge.

Some nodal or systemic disease is beyond the limits of detection using imaging studies.

Diagnosis and Evaluation

An abnormal digital rectal examination or an elevated serum PSA reading are indications for a prostate biopsy. The threshold PSA level for triggering a prostate biopsy is controversial. Until recently, the recommendation was to biopsy men with serum PSA of 4 ng/mL or more.[6,7] One of the limitations of PSA screening is its relatively low specificity. Age-specific reference ranges, PSA density, and free-to-total PSA ratios have been recommended to increase the specificity of PSA testing.[8] None of these efforts to increase the specificity of PSA testing has gained widespread acceptance. There is increasing evidence that a significant proportion of men with PSA levels between 2.5 and 4 ng/mL will have prostate cancer.[9] Men with PSAs in this range should undergo biopsy, determination of the ratio of free and total PSA, or careful follow-up.

Using biopsy to diagnose prostate cancer is also controversial. Hodge and colleagues[10] described a sextant biopsy technique that sampled the midsagittal peripheral zones. Several investigators have subsequently reported that a sextant biopsy represents inadequate sampling of the prostate for the detection of clinically relevant prostate cancer.[11,12] At present, most experts recommend a 12-core biopsy that samples both the midsagittal and lateral peripheral zones.

The evaluation of men with a diagnosed prostate cancer should be targeted to identify those men with lymph nodal or systemic metastases because these men are not considered candidates for curative intervention. Approximately 30% of men with T1 and T2 disease undergoing radical prostatectomy will ultimately develop biochemical recurrence over 15 years,[13] suggesting that in many cases the disease was beyond the surgical field at the time of radical prostatectomy. Unfortunately, in the cases not halted by radical prostatectomy, the nodal or systemic disease was beyond the limits of detection using imaging studies. In my practice, therefore, I generally do not obtain any imaging studies for men with clinically localized prostate cancer.[14] I obtain a radionuclide bone scan and a pelvic computed tomography (CT) only on those surgical candidates with a PSA above 15 or a Gleason score at or above 8. A ProstaScint® (Cytogen Corporation, Princeton, NJ) scan is obtained only on those men with equivocal pelvic node metastases on pelvic CT. I do not obtain any imaging studies to evaluate the local extent of the disease.

Treatment Options

The primary objective in the management of clinically localized prostate cancer is to cure the disease by total extirpation or destruction of the cancer, while preserving quality of life. The specific treatment options include radical prostatectomy, which can be

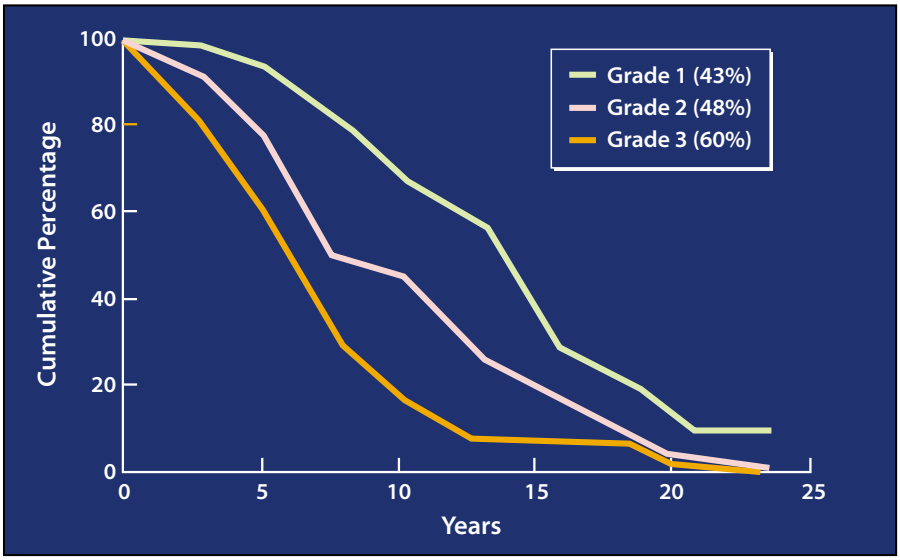


Figure 1. *Survival for men with localized prostate cancer managed with "watchful waiting." Inset shows ultimate risk of prostate cancer-related death. Reproduced with permission from Aus et al.*[17]

performed via the retropubic, perineal, or laparoscopic approach, and radiation therapy, which can be delivered using three-dimensional conformal external beam techniques or brachytherapy.

Prostate cancer can be cured only if there is no evidence of systemic or regional metastases and the disease is confined to the surgical field or the radiation template. Surgeons and radiation oncologists must make a concerted effort to exclude men with regional and systemic metastases who are unlikely to benefit from treatment. Because not all men with clinically localized prostate cancer will ultimately benefit from radical prostatectomy or radiation therapy, these therapies must be offered with both low short- and long-term complications and with good preservation of quality of life.

Selecting Candidates for Curative Interventions

The risk of prostate cancer to the host is dependent on life expectancy and the natural history of the cancer. The benefit of treatment is related to the ability to prevent metastasis and increase survival. The urologist and the radiation oncologist must make an assessment of both the natural history of the disease and the life expectancy of the host prior to recommending intervention for the treatment for localized disease. Information pertaining to life expectancy can be obtained from various life tables. Several reports in the literature have examined the natural history of prostate cancer. In practice, I typically refer to the life expectancy data presented in Table 1[15] and refer to the studies by Chodak and colleagues[16] and Aus and colleagues[17] (Figure 1) for insights regarding the natural history of the disease.

Based on this information, I would counsel a 65-year-old man that he has a 70% and 50% probability of surviving 10 and 15 years, respectively (Table 1). If this man has Grade 2 (Gleason score 5–7) adenocarcinoma, he is told that he has a 42% and 70% probability of developing systemic metastatic disease in 10 and 15 years, respectively, according to Chodak and colleagues[16] (Table 2) and approximately a 55% and 75% chance of dying of prostate cancer within 10 and 15 years, respectively, according to Aus and colleagues.[17] One limitation of these natural history studies is that nuclear grade was reported, not Gleason score. In the modern era, the grade of prostate cancers is reported using Gleason scores, not nuclear grade. Nevertheless, there does appear to exist a significant advantage to cure a 65-year-old man with a Grade 2 prostate cancer.

The benefit of treatment is based upon the ability to reverse the risk of developing metastases or death from prostate cancer. There are reliable 10- and 15-year estimates of survival data for radical prostatectomy and radiation therapy that provide insights into the effectiveness of these treatment options for curing prostate cancer.

Han and associates[13] have recently published their 15-year survival data

Table 2
Percentage of Men with Localized Prostate Cancer Treated Conservatively Who Developed Metastases at 10 and 15 Years: A Pooled Analysis

	Metastases, %	
Histologic Grade	10 Years	15 Years
1	19	40
2	42	70
3	74	85

Adapted from Chodak et al.[16]

Table 3
Survival Statistics for American Males Following Radical Prostatectomy (n=2404)

Recurrence	No. Men	Actuarial recurrence-free likelihood (95% CI) 5 Years	10 Years	15 Years
Overall	412	84 (83-86)	74 (71-76)	66 (61-70)
Isolated PSA elevation	234	92 (90-93)	85 (83-87)	79 (75-82)
Local	40	99 (99-100)	96 (95-97)	94 (92-96)
Distant ± local	138	96 (95-97)	90 (88-92)	82 (77-87)

Reproduced with permission from Han et al.[13]

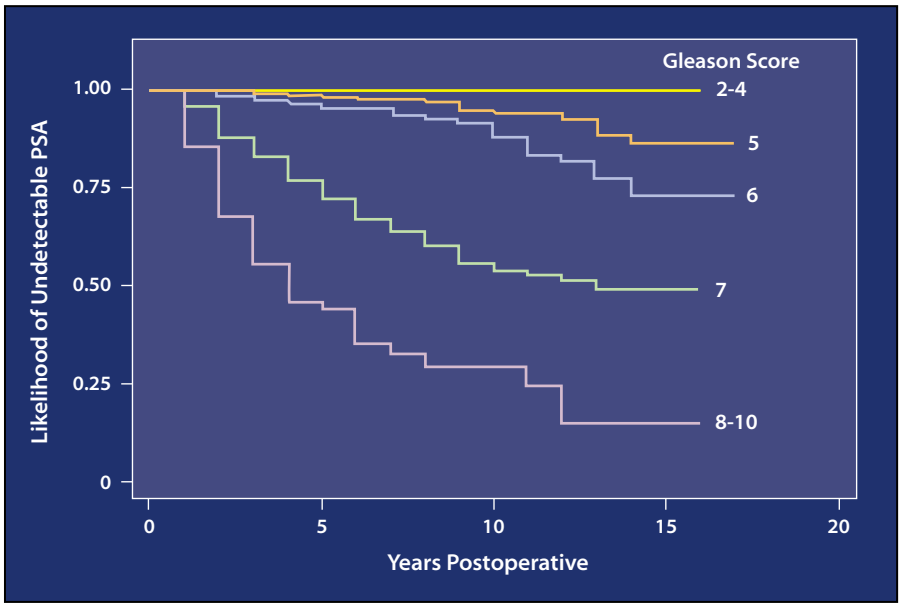
for a group of 2404 men who underwent radical prostatectomy between 1982 and 1999. It is important to recognize that a significant subset of these men was diagnosed in the pre-PSA era, because only 36% of the total cases were T1c disease. In more contemporary radical prostatectomy series from the 1990s, approximately 80% of tumors are T1c cancers.[18] Tumors that are impalpable (T1c) have been shown to have lower tumor volume and less likelihood of extracapsular extension compared to palpable tumors (T2 disease).[19] A disproportionate number of men contributing to the 10- and 15-year survival analysis reported by Han and associates[13] had palpable disease. The 5-, 10-, and 15-year actuarial progression-free rate for overall progression, biochemical recurrence only, local recurrence, and distant with or without local recurrence reported by Han and associates[13] is presented in Table 3. Overall, the probability of developing systemic metastases within 10 and 15 years for the entire group was 90% and 82%, respectively. Baseline serum PSA, postoperative Gleason score, clinical stage, and pathologic stage were all predictors of recurrence-free survival. The impact of Gleason score on biochemical-recurrence–free survival is shown in Figure 2. The 10-year biochemical-recurrence–free survival for men with Gleason score 6 tumors was 88%.

Bagshaw[20] has reported long-term survival following external beam radiotherapy in a cohort of men treated between 1956 and 1990. Therefore a significant subset of these men was diagnosed in the pre-PSA era. For men with T1 and T2a disease, the 10-, 15-, and 20-year disease-specific survival was approximately 85%, 70%, and 60%, respectively (Figure 3). Disease-free survival was not based upon biochemical failure. It is important to note that a significant proportion of men developed disease recurrence between 10 and 20 years' follow-up.

The Northwest Hospital (Seattle) experience[21] has recently been reported with 12-year survival data for men undergoing brachytherapy. It is important to recognize that all of the men were diagnosed in the PSA era. In general, men with Gleason scores between 2 and 6 and PSA levels below 10 ng/mL were offered brachytherapy alone, whereas men with Gleason scores between 7 and 10 and PSA at or above 10 ng/mL were offered a combination of brachytherapy and external beam therapy. The overall 12-year disease-free survival of the 2 groups combined was 70%. It is interesting that the 12-year disease-free survival rates for the monotherapy and the combination groups were 66% and 79%, respectively. The disease-free survival plot for the brachytherapy-alone group is shown in Figure 4.

The only way to definitively compare radiation therapy and radical prostatectomy for the treatment of clinically localized prostate cancer is to perform a randomized study. The only randomized study comparing these 2 options showed a survival

Figure 2. *Kaplan-Meier actuarial likelihood of prostate-specific antigen (PSA) recurrence by Gleason score following radical prostatectomy. From Han et al,[13] reproduced with permission.*



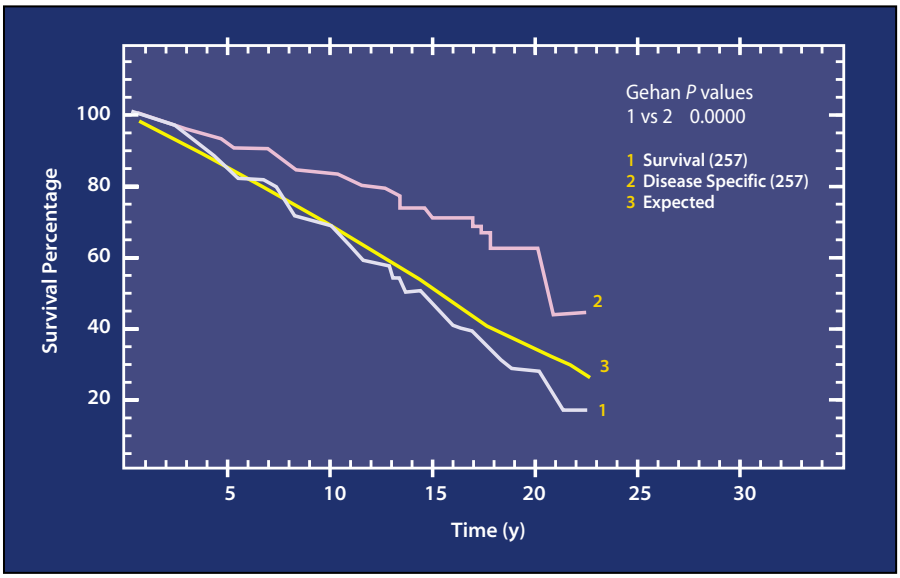
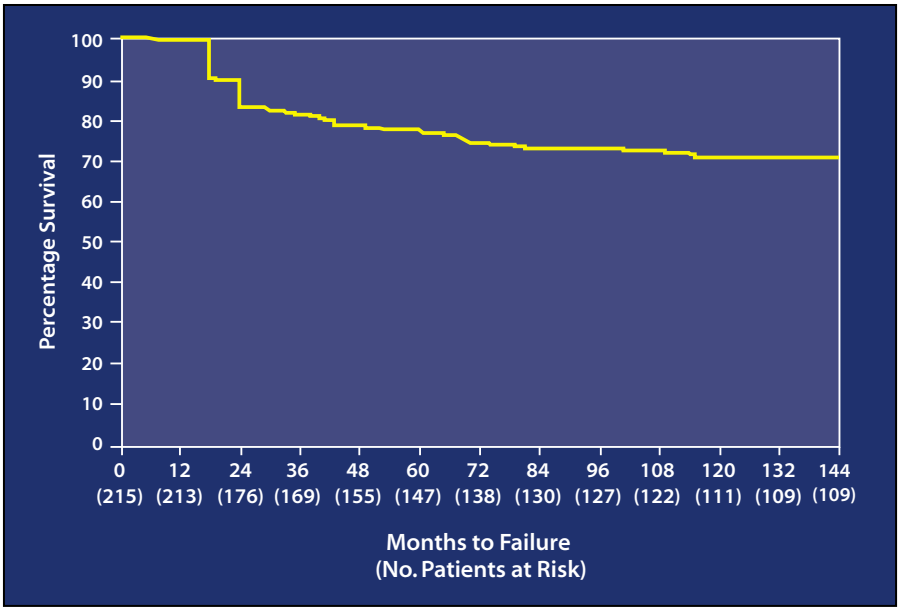


Figure 3. *Kaplan-Meier survival following external beam radiotherapy. Reproduced with permission from Bagshaw.*[20]

advantage for radical prostatectomy,[22] although this study has significant flaws. In the absence of other randomized studies, clinically useful data can be obtained by comparing survival data in cohorts of men with comparable tumor characteristics treated with radical prostatectomy or radiation during the same time period.

On a first-glance comparison of the Han[13] and the Northwest Hospital[21] data, it may appear that the 10-year, disease-free, biochemical recurrence–free survival is similar for radical prostatectomy (74%) and brachytherapy (60%) series. There are several caveats that must be considered when comparing these survival data reports. First, the definitions for biochemical-recurrence–free survival are different in surgical and radiation therapies series. The definition for biochemical progression in the series reported by Han and colleagues is a PSA above 0.2 ng/dL, whereas in the brachytherapy series from the Northwest Hospital, the definition was 3 consecutive rises in serum PSA level measured at least 6 months apart. The definition of biochemical-recurrence–free survival favors the radiation therapy group. In the Han series, the overwhelming majority of men with follow-up data at 10 and 15 years were diagnosed in the pre-PSA era and therefore include a higher proportion of men with palpable disease. Han and colleagues[23] have recently reported that tumors in the Han series diagnosed in the pre-PSA era (prior to 1992) had a much lower probability of being impalpable, a much greater probability of extracapsular extension, and less favorable biochemical-recurrence–free and disease-free survival. It is also important to recognize that a significant proportion of men in the radiation series received a combination of hormonal therapy, external beam, and brachytherapy. Han and colleagues[23] also reported that the biochemical-recurrence–free survival at 10 years following radical prostatectomy for men diagnosed in 1982–1988 versus 1989–1991 was 62% and 80%, respectively. Ten-year survival data were not available for men diagnosed since 1992. The biochemical-disease–free survival at 10 years following radical prostatectomy for all cancers diagnosed between 1989 and 1991 is far superior to the 66% biochemical-recurrence–free survival for Gleason 2–6 cancers undergoing brachytherapy during a similar time interval. Thus, when one compares men diagnosed in the same period with Gleason scores favoring brachyther-

Figure 4. *Disease-free survival following brachytherapy. The number of men who were available for evaluation is shown in parenthesis. From Korb and Brawer.*[21]



apy, radical prostatectomy appears to be superior to radiation therapy in total eradication of localized disease.

Complications of Therapy

It is important to balance the likelihood that treatment will prevent metastases and death from prostate cancer against the risks of intervention. Fortunately, morbidity and mortality of both radical prostatectomy and radiation therapy are low owing to significant advances in technique.

Shekarriz and colleagues[24] recently reviewed the complications of several radical prostatectomy series reported in the 1990s. In the hands of experienced surgeons and properly selected candidates, the likelihood of technical and medical intraoperative complications is exceedingly low. Shekarriz and colleagues reported that the incidence of rectal injuries varied between 0.05% and 2.9%, ureteral injuries varied between 0% and 1.6%, deep vein thrombosis varied between 0.6% and 7.8%, pulmonary embolisms varied between 0.7% and 2.7%, myocardial infarction arrhythmias varied between 0% and 1.8%, lymphoceles varied between 0.4% and 22.3%, and wound complications varied between 0% and 2.6%.

Lepor and colleagues[18] recently reviewed a consecutive series of 1000 radical retropubic prostatectomies performed between 1994 and 1999. The intraoperative, perioperative, and postoperative complications are presented in Table 4. This large personal series demonstrates the extremely low morbidity associated with radical prostatectomy in the modern era. In this study, the overall risk of allogeneic transfusion was 9.8%. The average length of hospital stay was 2.3 days, the reoperation rate was 0.5%, and the hospital readmission rate was 1.5%. Lepor and colleagues[18] strongly encourage men to return to unlimited physical activity within 21 days of radical prostatectomy. Figure 5 shows a 57-year-old patient (no. 794, center) who ran in the U.S. National Track and Field finals 17 days after radical prostatectomy and placed third in the race.

Table 4
Radical Prostatectomy: A Consecutive Series of 1000 Radical Retropubic Prostatectomies

Complications	Percentage
Intraoperative rectal injury	0.5
Perioperative (inpatient)	
Myocardial infarction	0.3
Pulmonary embolisms	0.3
Postoperative (discharge 30 d)	
Stricture	1.0
Wound complication	0.8
Urinary retention	0.7
Clot urinary retention	0.3

Adapted from Lepor et al.[18]

Because the intraoperative, postoperative, and perioperative complications associated with radical prostatectomy are quite low, the primary limitation of radical prostatectomy is its impact on quality of life. Urinary incontinence and erectile dysfunction are significant concerns of men who are undergoing radical prostatectomy.

The incidence reported in the literature of urinary incontinence following radical prostatectomy ranges between 5% and 31%.[25–34] The wide range can be attributed to differences in definitions of continence, methodology for assessing continence, time intervals between surgery and evaluation of continence, ages of the patient populations, and level of expertise of the surgeon. It has been well demonstrated that the most reliable assessment of continence is achieved when using validated patient questionnaires.[34] Final continence status should be assessed at least 1 year following radical prostatectomy, because this has been shown to be the time required to achieve maximal continence.[25,30,34]

It is also important to differentiate between perfect urinary control and continence. The majority of men who have minimal stress incontinence precipitated by very heavy activity and those who use a single small protective pad over a 24-hour period gen-

Figure 5. *Seventeen days after radical prostatectomy, this 57-year-old man (no. 794, center) competed in the U.S. National Track and Field finals.*

erally consider themselves continent. Between 20% and 33% of men will require some use of pads following radical prostatectomy, based on surveys using validated patient questionnaires.[31–34] Using the definition of continence of none or a single small pad use over a 24-hour interval, between 87% and 95% of men achieve urinary continence following radical prostatectomy.[31–34] It is important to perform a video urodynamic evaluation on all men who do not achieve continence because in selected cases detrusor instability or an anastomotic stricture may be the cause of incontinence.[35] Both of these conditions can be successfully treated with subsequent improvement in continence. For the occasional individual who has severe stress incontinence, an artificial urinary sphincter can be placed with excellent results.

It is important to perform a video urodynamic evaluation on all men who do not achieve continence.

Prior to the introduction of nerve-sparing radical retropubic prostatectomy, erectile dysfunction was virtually assured following radical prostatectomy. Potency rates currently reported in community-based surveys are typically less than 30%.[27,31] Experts report potency rates between 20% and 80%.[36–38] The ability to preserve potency is related to the patient's age, baseline sexual performance, and whether the neurovascular bundles can be preserved.[36] It is also important to assess potency at least 18 and preferably 24 months after radical prostatectomy,[39,40] and imperative to utilize validated patient questionnaires to achieve reliable outcome data.[41] Several expert surgeons evaluating the CaverMap device (UroMed Corp., Boston, MA) evaluated potency using patient-completed questionnaires that were mailed and scored by a third party.[42] Potency was reported at only 12 months, which underestimates the final potency status. In this study, 70% of men self-reported the ability to achieve erections adequate for intercourse.

There are several very effective ways to manage erectile dysfunction following radical prostatectomy. In practice, I advise low-dose sildenafil every evening and a monthly 100-mg dose prior to sexual activity. We also encourage men who wish to resume having intercourse to begin penile injection therapy. Many men who fail to gain unassisted erection will have very good sexual intimacy without intercourse or will find a satisfactory way to achieve an erection adequate for intercourse.

Because of the close proximity of the rhabdosphincter, neurovascular bundles, bladder, and rectum to the prostate, complications related to potency, continence, and bladder and bowel function are potential problems associated with radiotherapy of prostate cancer. Over the last decade, efforts have been made to decrease the complications following radiation therapy by developing three-dimensional conformal radiation therapy (3D-CRT) planning systems and by developing techniques to place interstitial seeds more precisely with improved dosimetry using ultrasound guidance. It is difficult to determine the true impact of radiation therapy on outcomes due to the ambiguity of the grading system that is accepted by the Radiation Therapy Oncology Group (RTOG). The grading of complications ranges from 0 to 5. Grade 1 is a minor symptom requiring no treatment; Grade 2 is a minor symptom that requires medication; Grade 3 is a symptom requiring minor surgical intervention; Grade 4 is a symptom requiring major surgical intervention; and Grade 5 is death.[43] If a patient has significant urinary incontinence or urinary urgency and undergoes no medical or surgical intervention, then this outcome would be a Grade 1 complication. Another problem with reporting complications in the literature is that many studies report Grade 0 and 1 complications together, making it difficult to discriminate between lack of symptoms and minor symptoms. Another significant limitation of the majority of outcome data following radiation therapy is the failure to use validated patient questionnaires.

Michalski and colleagues[44] recently reported on toxicity following 3D-CRT for prostate cancer in 592 men randomized to an RTOG study comparing different dosing regimens. Groups 1 and 2 had clinically localized prostate (T1 and T2) disease: Group 1 had less than 15% probability of seminal vesicle (SV) involvement and Group 2 had a 15% or higher probability of SV involvement. The planning target volume for Group 2 included the SV. Minimum prescription dose began at 68.4 Gy (level I) and was escalated to 73.8 Gy (level II). The acute bladder and bowel toxicities are shown in Figure 6. Approximately 50% of men experienced acute bladder or bowel toxicity. Overall, 45% and 35% of men in Groups 1 and 2 developed a Grade 2 acute morbidity, respectively.

Zelefsky and colleagues[45] recently reported the late complications following 3D-CRT in 137 men and brachytherapy in 145 men with favorable-risk prostate cancer who were treated between 1988 and 1997. This report represents a small proportion of these men actually treated at Memorial Sloan-Kettering Cancer

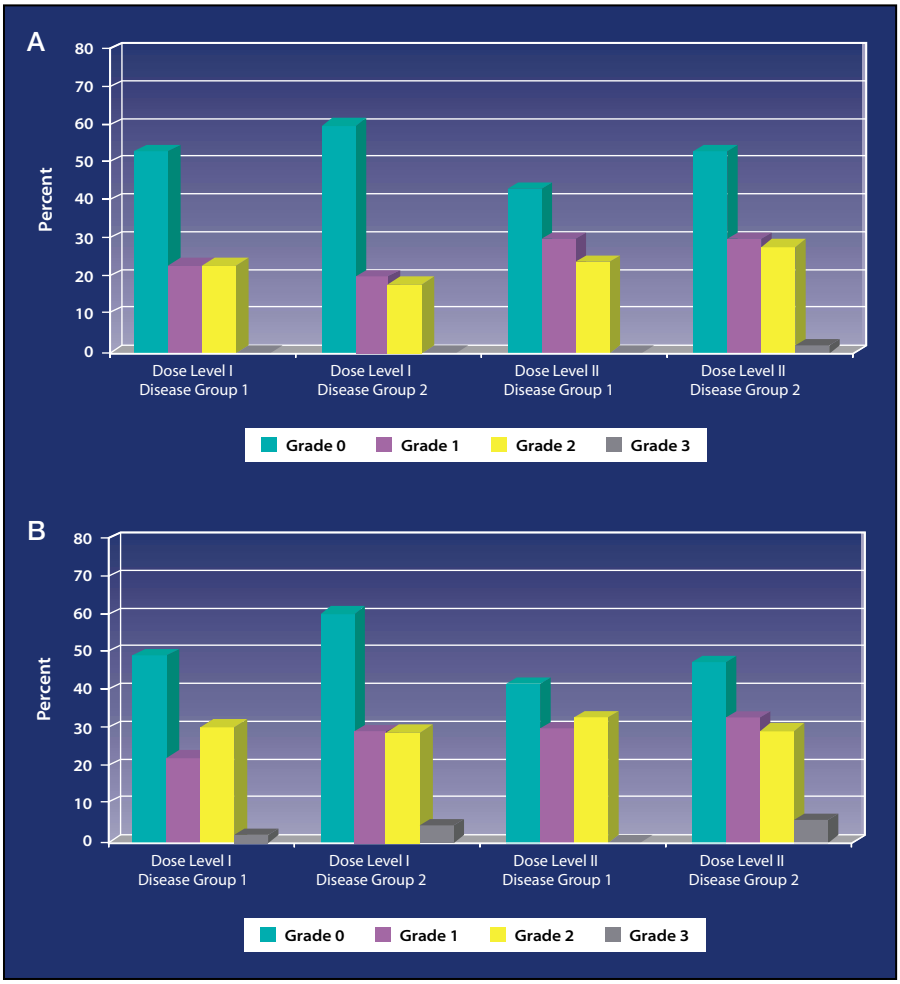


Figure 6. *Acute bowel* **(A)** *and bladder* **(B)** *toxicities following three-dimensional conformal radiotherapy. From Michalski et al,[44] reproduced with permission.*

Center during this time period. Late treatment complications were defined as events developing 90 days after completion of radiation therapy or those events persisting beyond 90 days after completing radiation therapy. Patient questionnaires were not used to capture complications. Nine percent and 38% of men developed Grade 2 or 3 urinary toxicity following 3D-CRT and brachytherapy, respectively, and 6% and 4% of men developed Grade 2 rectal toxicity following 3D-CRT and brachytherapy, respectively. Five years following treatment, 43% of men who underwent 3D-CRT and 53% of men who underwent brachytherapy complained of erectile dysfunction.

Talcott and colleagues[46] recently reported the first long-term outcome assessment following brachytherapy for early prostate cancer using a validated patient questionnaire. A questionnaire assessing urinary and bowel function was mailed to 166 men who were treated at Northwest Hospital with brachytherapy and who had at least 2 years' and 9 months' follow-up. Of the 132 men who were later contacted, 80% completed the questionnaire; 15% of men who underwent seed implantation alone and 19% who underwent a combination of seed implantation and external beam therapy complained of frequent diarrhea, mucus per rectum, or rectal bleeding, whereas 40% of men who underwent seed implantation alone and 55% who underwent seed implantation and external beam radiation complained of urinary leakage. As previously discussed, absolute urinary control is not a requirement for continence. The use of pads is a better discriminator as to the level of continence and its impact on quality of life. Eighteen percent of men who underwent seed implantation alone and 13% who underwent seed implantation and external beam therapy required pad use for their incontinence. A history of prior transurethral radical prostatectomy was not an exclusionary factor, and this is known to increase the rate of incontinence. Sexual dysfunction was a significant problem following brachytherapy; 68% of men who underwent seed implantation alone and 82% who underwent seed implantation and external beam therapy indicated that their erections were inadequate for penetration without manual assistance.

Brandeis and colleagues[47] reported a study comparing quality-of-life outcomes following radical prostatectomy and brachytherapy using a validated patient questionnaire for men treated at a single institution. Follow-up ranged between 3 and 17 months. An obvious limitation of this study is that continence status following radical prostatectomy improves throughout the first postoperative year and potency improves throughout the first 2 postoperative years, whereas sexual dysfunction and urinary incontinence are late complications following radiation therapy. Therefore, the relatively short follow-up interval significantly underestimates the complications of brachytherapy and overestimates the

complications of surgical intervention. In this study, radical prostatectomy had a greater negative impact on incontinence compared with brachytherapy or controls. Interestingly, an assessment of both continence and voiding dysfunction showed that brachytherapy had a greater negative impact than radical prostatectomy, and radical prostatectomy was equivalent to controls. Bowel function was a greater bother with brachytherapy compared with both radical prostatectomy and controls. Sexual function was equivalent in brachytherapy and radical prostatectomy groups, and both treated groups were worse than controls. Based upon the UCLA comparative experience and the composite experience reported in the literature, it appears that radical prostatectomy, 3D-CRT, and brachytherapy have an overall similar impact on quality of life (see Table 5).

Table 5
Quality-of-Life Outcomes Following Brachytherapy

Outcome	Seed Implants Alone (%)	Seed Implants and External Beam Therapy (%)
Frequent diarrhea, mucus per rectum, or rectal bleeding	15	19
Urinary leakage	40	55
Pad use for incontinence	18	13
Inadequate erection for penetration without manual assistance	68	82

Adapted with permission from Talcott et al.[46]

Conclusions

With the widespread acceptance of PSA screening, a greater proportion of men are being diagnosed with clinically localized prostate cancer. Both radical prostatectomy and radiation therapy have proven curative value for a significant subset of men with localized prostate cancer. Survival outcomes indicate that radical prostatectomy is a more reliable cure than radiation therapy for clinically localized prostate cancer. Overall, the immediate treatment-related morbidity of radical prostatectomy and radiation therapy in the modern era is quite low. Radical prostatectomy and radiation therapy appear to have a similar impact on continence and erectile function. Rectal dysfunction represents morbidity unique to radiation therapy.

There are several opportunities to improve outcomes following the treatment of localized prostate cancer. Early detection is of paramount importance for success of radical prostatectomy and radiation therapy. PSA screening should be highly encouraged. Efforts should be made to identify better screening tools. For those men who are diagnosed with clinically localized prostate cancer, a significant subset will have micrometastases that are undetectable using current imaging studies. It is unlikely that technology will achieve the level of imaging discrimination to identify these occult metastases. Efforts should be directed towards molecular profil-

Main Points

- There is increasing evidence that a significant proportion of men with prostate-specific antigen (PSA) levels between 2.5 and 4 ng/mL will have prostate cancer; men with PSAs in this range should undergo biopsy, determination of the ratio of free and total PSA levels or careful follow-up.
- Most experts recommend a 12-core biopsy that samples both the midsagittal and lateral peripheral zones.
- Approximately 30% of men with T1 and T2 disease undergoing radical prostatectomy will ultimately develop biochemical recurrence over 15 years.
- Tumors that are impalpable (T1c) have been shown to have lower tumor volume and less likelihood of extracapsular extension compared with palpable tumors (T2 disease).
- Comparing men diagnosed in the same period with Gleason scores favoring brachytherapy, radical prostatectomy appears to be superior to radiation therapy in total eradication of localized disease; morbidity and mortality of both radical prostatectomy and radiation therapy are low owing to significant advances in technique.
- The ability to preserve potency after radical prostatectomy is related to the patient's age, baseline sexual performance, and whether the neurovascular bundles can be preserved.
- It appears that radical prostatectomy, three-dimensional conformal radiation therapy, and brachytherapy have an overall similar impact on quality of life.

ing of tumors, so that their metastatic potential can be more accurately predetermined. Surgical and radiation therapy delivery techniques can be further improved in order to decrease the likelihood of treatment-related morbidity, especially on quality-of-life outcomes. In addition, more effective ways for treating incontinence and erectile dysfunction can limit the impact of these problems on quality of life. Finally, there is a need for neoadjuvant and adjuvant therapies that can be utilized in those cases where radical prostatectomy and radiation are less likely to completely eradicate or destroy the cancer. ■

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